

## **REMARKS**

Applicants respectfully request reconsideration and allowance of all pending claims.

### **I. Status of Claims**

Claims 1, 6-7, 11, 14, 17, 27, 30, 35-37, 41-42, 44, 47, and 50-55 will be pending upon entry of this Amendment B and Response to Office Action.

In this Amendment B, claims 1, 7, 27, and 30 have been amended to require the catalyst to be a precious metal catalyst. Support for the amendment to these claims may be found, for example, in the original specification as published (U.S. Publication No. 2006/0025588) at paragraph [0032]. Additionally, claims 54 and 55 have been added to call for the process to be carried out in the presence of hydrogen gas. Support for these new claims may be found, for example, in original claim 35, as well as in the original specification published at paragraph [0031].

Finally, Applicants respectfully point out that claim 14 was amended in Preliminary Amendment A (filed June 3, 2005) to depend from claim 7. However, as published, claim 14 of the instant application remains dependent upon claim 37 as originally filed. Support for this amendment may be found, for example, in the specification at paragraph [0036].

### **II. Obviousness Type Double Patenting Rejection**

Claims 1, 6-7, 11, 14, 17, 27, 30, 35-37, 41-42, 44, 47, and 50-53 have been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-72 of copending Application No. 10/594,486 (Jarvi, et al.).

Applicants note that this rejection is a provisional obviousness-type double patenting rejection, since the later-filed U.S. Patent Application No. 10/594,486 has not yet issued as a patent. Accordingly, Applicants respectfully reserve the right to address

the merits of this rejection, as appropriate, if the listed application issues as a patent before the application at hand.

## II. 35 U.S.C. 102 Rejections

Reconsideration is requested of the rejection of claims 1, 6-7, and 11 under 35 U.S.C. §102(b) as being anticipated by (i) George, et al. (U.S. Patent No. 4,847,263), and (ii) George, et al. (U.S. Patent No. 4,808,594). Reconsideration is additionally requested of the rejection of claims 1, 6-7, and 11 under 35 U.S.C. §102(e) as being anticipated by Schloemer, et al. (U.S. Patent No. 6,861,525).

### (A) The Claimed Subject Matter

Claim 1, from which claim 6 depends, is directed, in relevant part, to a process for the preparation of a heteroaryl acetamide of Formula 1A (as detailed above) from a heteroaryl  $\alpha$ -hydroxyacetamide of Formula 1 (also as detailed above). The process comprises directly hydrogenating the noted heteroaryl  $\alpha$ -hydroxyacetamide in the presence of a strong acid, a halide, and a **precious metal catalyst** (*emphasis added*).

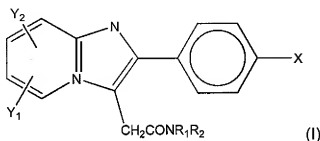
Claim 7, from which claim 11 depends, is directed, in relevant part, to a process for the preparation of an imidazopyridine acetamide of Formula 6A (as detailed above) from an imidazopyridine  $\alpha$ -hydroxyacetamide of Formula 6 (also as detailed above). The process comprises directly hydrogenating the noted imidazopyridine  $\alpha$ -hydroxyacetamide in the presence of a strong acid, a halide, and a **precious metal catalyst** (*emphasis added*).

Notably, the processes as claimed in the instant application are carried out in a **direct** hydrogenation step; that is, the heteroaryl  $\alpha$ -hydroxyacetamide is directly reduced without first forming and/or isolating a halogenated intermediate compound. This direct hydrogenation is achieved using a mixture of a strong acid, a halide, and **precious metal catalyst**. (See, e.g., paragraph [0036].) More particularly, as disclosed in the exemplary embodiments of working Examples 1-5, a solution of concentrated sulfuric acid, diluted with glacial acetic acid, was stirred into a reactor, along with a

mixture of LiBr, water, and 5% Pd/BaSO<sub>4</sub> catalyst, to directly reduce α-hydroxy zolpidem to form zolpidem.<sup>1</sup> Nowhere is it stated that the α-hydroxy zolpidem is first reacted to form a halogenated intermediate compound that is isolated, which then further reacted with the other reagents to form the reduced zolpidem.

(B) The Cited Art

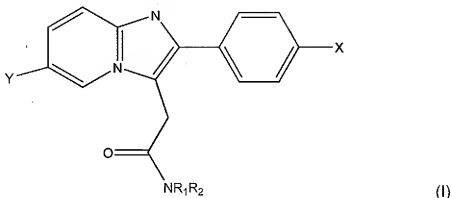
George, et al. ("263) disclose imidazo[1,2-a]pyridine derivatives of the general formula (I):



wherein Y<sub>1</sub>, Y<sub>2</sub>, X, R<sub>1</sub> and R<sub>2</sub> are as defined, for example, in the Abstract or column 1 at lines 19-26. The disclosed derivatives are prepared using a multi-step process to reduce the hydroxy-substituted compound (e.g., compound (VII) at the bottom of column 8), which involves first forming an isolatable hydrogenated compound. For example, in one embodiment, the derivative is formed using the multi-step reaction scheme of Appendix 1 (at the bottom of columns 7 and 8), wherein: (a) the hydroxy-substituted compound of formula (VII) is first treated using SOCl<sub>2</sub>, and then (b) the resulting chloro-substituted compound is reduced *in situ* with a subsequently added agent, such as Rongalite, to obtain the compound (VIII). Notably, in the reduction of compound (VII) to compound (VIII), compound (VII) is **not directly hydrogenated in the presence of a precious metal catalyst**. In fact, no reference is even made by George, et al. to a metal catalyst of any kind.

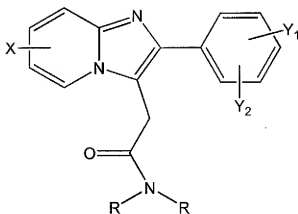
<sup>1</sup> See also Examples 6, 7, 13-15, in which concentrated solutions of sulfuric acid, diluted with glacial acetic acid, are mixed with NaBr and 5% Pd/BaSO<sub>4</sub> catalyst to directly reduce α-hydroxy zolpidem to form zolpidem. Similarly, in Example 10, a sample of O-acetate, dissolved in glacial acetic acid, was mixed with sulfuric acid, NaBr, and 5% Pd/BaSO<sub>4</sub> catalyst to form zolpidem. In Example 12, a sample of O-propionate, dissolved in glacial acetic acid, was mixed with sulfuric acid, NaBr, and 5% Pd/BaSO<sub>4</sub> catalyst to form zolpidem. Similar reactions are depicted in working Examples 16-20.

Similarly, George, et al. ('594) disclose an imidazopyridine of the general formula (I):



wherein X, Y, R<sub>1</sub> and R<sub>2</sub> are as defined, for example, in the Abstract or column 1 at lines 7-25. The disclosed imidazopyridines are prepared using a multi-step process to reduce the hydroxy-substituted compound (e.g., compound (IX) at column 7, lines 25-35), which involves first forming an isolatable hydrogenated compound. For example, in one embodiment, the imidazopyridine is formed using the multi-step reaction scheme of Appendix 2 (column 6, line 55 to column 7, line 45), wherein: (a) the hydroxyl-substituted compound of formula (IX) is first reacted with thionyl chloride, and then (b) the resulting chloro-substituted compound is reduced using a subsequently added agent, such as Rongalite, to obtain the compound (I). Notably, in the reduction of compound (IX) to compound (I), compound (IX) **is not directly hydrogenated in the presence of a precious metal catalyst**. In fact, no reference is even made by George, et al. to a metal catalyst of any kind.

Schloemer, et al. ('525) disclose a process for producing imidazo[1,2-a]pyridine-3-acetamides of structural formula (I):



(II)

wherein X, Y<sub>1</sub>, Y<sub>2</sub>, and R are as defined, for example, in column 2 at lines 37-41. The disclosed acetamides are prepared by reacting an imidazo[1,2-a]pyridine with a hydroxy-substituted compound of formula (II) (see column 7 at lines 20-25), to produce an intermediate hydroxy-substituted compound of formula (III) (see column 7 at lines 25-35). The compound of formula (III) is subsequently reacted with phosphorous tribromide to obtain the compound of formula (I). Notably, in the reduction of compound (III) to compound (I), compound (III) **is not hydrogenated in the presence of a precious metal catalyst**. In fact, no reference is even made by Schloemer, et al. to a metal catalyst of any kind.

**(C)      The Claimed Subject Matter is Not Anticipated**

MPEP §2131 states that "a claim is anticipated only if **each and every element** as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." As noted above, the '263 patent and the '594 patent of George, et al., as well as the '525 patent of Schloemer, et al., fail to disclose hydrogenating a heteroaryl α-hydroxyacetamide in the presence of a strong acid, a halide, **and a precious metal catalyst**, in order to form a heteroaryl acetamide. In fact, these patents do not even reference the use of a metal catalyst of any kind. The cited patents clearly fail to disclose each and every element of Applicants' claim 1, or claim 7. As such, these claims are not anticipated by the cited patents.

Claim 6 depends from claim 1, and as such, claim 6 is not anticipated by the cited references for the same reasons as claim 1 set forth above, as well as for the additional elements it requires.

Claim 11 depends from claim 7, and as such, claim 11 is not anticipated by the cited references for the same reasons as claim 7 set forth above, as well as for the additional elements it requires.

### **III. 35 U.S.C. 103(a) Rejection**

Reconsideration is requested of the *separate* rejection of claims 14, 17, 27, 30, 35-37, 41-42, 44, 47, and 50-53 under 35 U.S.C. §103(a) as being unpatentable in view of George, et al. (U.S. Patent No. 4,847,263), George, et al. (U.S. Patent No. 4,808,594), or Schloemer, et al. 6,861,525.

#### **(A) The Claimed Subject Matter**

Claims 14, 17, 27, and 30 depend from claim 7, which is discussed above. In the interests of brevity, the details of claim 7 will therefore not be repeated here.

Claim 35, from which claims 36-37, 41-42, 44, 47, and 50-53 depend, is directed to, in relevant part, a process for the preparation of an imidazopyridine acetamide of Formula 7A (as detailed above) from an imidazolpyridine  $\alpha$ -hydroxyacetamide of Formula 7 (also as detailed above). The process comprises directly hydrogenating the noted imidazopyridine  $\alpha$ -hydroxyacetamide in the presence of a **hydrogen gas**, a strong acid or mixture of strong acids with a pKa of about -9 or less, a chloride or bromide ion, and a **palladium catalyst** (*emphasis added*).

#### **(B) The Cited Prior Art**

The cited prior art is discussed in detail above. Accordingly, in the interests of brevity, the cited prior art will not be discussed again here. However, Applicants additionally point out that, not only does each reference **fail to disclose or suggest the use of a precious metal catalyst**, or a metal catalyst of any kind, but each reference

also **fails to disclose or suggest the use of hydrogen gas** in the reduction reaction to prepare the compound of interest.

**(C)      The Claimed Subject Matter is Not Obvious**

As set forth in M.P.E.P. §2143, in order for the Office to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) the prior art reference, when modified, must teach each and every element of the claim; (2) there must be some suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference; and (3) there must be some reasonable expectation of success. For the reasons set forth in detail below, Applicant respectfully submits the Office has failed to establish a *prima facie* case of obviousness, because (i) each and every element of the claims have not been disclosed or suggested by the cited references, and/or (ii) no reason is provided to modify the disclosure of the cited references to arrive at the processes of Applicants' claims. It simply would not have been obvious to one skilled in the art to arrive at Applicants' claimed process.

As noted above, Applicants submit each of the cited references, both alone and in combination, **fail to disclose or suggest** directly hydrogenating an imidazopyridine  $\alpha$ -hydroxyacetamide in the presence of a strong acid, a halide, and a **precious metal catalyst** to form an imidazopyridine acetamide. Furthermore, with respect to claim 35, each of the cited references, again both alone and in combination, also **fail to disclose or suggest** directly hydrogenating an imidazopyridine  $\alpha$ -hydroxyacetamide in the presence of a strong acid, a halide, a **precious metal catalyst, and hydrogen gas**, to form an imidazopyridine acetamide. Notably, the cited references do not even reference the use of a precious metal catalyst or hydrogen gas. Accordingly, the cited references, both alone and in combination, clearly **fail to disclose or suggest each and every element** of the claims.

Applicants additionally submit there is no reason to modify the disclosure provided in the cited references to arrive at the process of the rejected claims.

More specifically, Applicants respectfully submit there is no reason to modify the cited references in view of the **total silence** of the cited references with respect to the use of a **precious metal catalyst**, optionally in combination with **hydrogen gas** (as in the case of claim 35).

In view of the foregoing, Applicants respectfully submit claims 7 and 35 are patentable over the cited references, both alone and in combination. Claims 14, 17, and 27 depend from claim 7 and further, claims 36-37, 41-42, 44, 47, and 50-53 depend from claim 35 and are therefore submitted as patentable over the cited references for the same reasons as set forth for claims 7 and 35, as well as for the additional elements they require.

### **CONCLUSION**

In view of the foregoing, Applicants respectfully request favorable reconsideration and allowance of all pending claims.

Applicants do not believe that a fee is due in connection with the submission of this Amendment B and Response to Office Action. If, however, the Commissioner determines that a fee is due, authorization is hereby given to charge Deposit Account No. 13-1160.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Craig Simán", with a long horizontal flourish extending to the right.

Craig D. Simán, Reg. No. 60,137

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